

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A ~~eartridge composition~~ comprising a ~~formation~~chondrogenesis stimulator containing a an isolated membrane-bound transferrin-like protein (MTf).

2. (Currently Amended) The ~~ehondrogenesis stimulator~~ composition according to claim 1, wherein the isolated MTf is selected from the group consisting of ~~rabbit p76 protein,~~ human p97 protein, and ~~a~~ an isolated protein demonstrating ~~the MTf~~ an activity of membrane-bound transferring protein for stimulating chondrogenesis activity that has an amino acid sequence encoded by DNA which hybridizes, under stringent conditions that consist of hybridization at 68 C in a solution containing 6 X SSC, 0.5% SDS, 10 mM EDTA, 5 Denhardt's solution and 10 mg/ml of denatured salmon sperm DNA, with a DNA coding for ~~p76 protein~~ or a p97 protein.

3. (Currently Amended) The ~~ehondrogenesis stimulator~~ composition according to claim 1, wherein the isolated MTf is selected from the following:

1) ~~a protein having the amino acid sequence of SEQ~~

~~ID NO: 2,~~

2) ~~a~~ an isolated protein having the amino acid

sequence of SEQ ID NO: 4;

~~3) a protein having the amino acid sequence of SEQ
ID NO: 15; and~~

4) ~~a~~ an isolated protein demonstrating the MTf activity that has an amino acid sequence encoded by DNA which hybridizes, under stringent conditions that consist of hybridization at 68 C in a solution containing 6 X SSC, 0.5% SDS, 10 mM EDTA, 5 Denhardt's solution and 10 mg/ml of denatured salmon sperm DNA, with a DNA encoding the protein of SEQ ID NO: ~~2, 4 or 15~~.

4. (Currently Amended) The ~~chondrogenesis stimulator composition~~ according to claim 2, wherein the MTf is isolated human p97 protein.

5. (Currently Amended) A ~~chondrogenesis stimulator composition~~ containing soluble isolated MTf.

6. (Currently Amended) The ~~chondrogenesis stimulator composition~~ according to claim 5, wherein the soluble isolated MTf lacks the GPI anchor region.

7. (Original) An agent for gene therapy to promote chondrogenesis which contains as an active ingredient an expression vector incorporating a DNA encoding any one of the following proteins:

- 1) a protein having the amino acid sequence of SEQ ID NO: 2;
- 2) a protein having the amino acid sequence of SEQ ID NO: 4;
- 3) a protein having the amino acid sequence of SEQ ID NO: 15;

4) a protein demonstrating the MTf activity that has an amino acid sequence encoded by DNA which hybridizes, under stringent conditions, with a DNA coding for the protein of SEQ ID NO: 2, 4 or 15; and

5) a protein which is the same as protein 1), 2), 3) or 4), except that it lacks the GPI anchor region.

8. (Currently Amended) A composition comprising
~~The the~~ chondrogenesis stimulator according to claim 1 ~~which~~
~~is used in combination with~~ and an MTf activating agent.

9. (Currently Amended) A composition comprising
~~The the~~ chondrogenesis stimulator according to claim 1 ~~which~~
~~is used in combination with~~ and insulin or an insulin-like growth factor.

10. (Cancelled)

11. (Original) A chondrogenic differentiation suppressing agent containing an MTf antagonist.

12. (Original) The chondrogenic differentiation suppressing agent according to claim 11, wherein the MTf antagonist is an anti-MTf antibody or an oligonucleotide or an oligonucleotide analog that are hybridizable with a nucleic acid encoding MTf.

13. (Original) A method for screening an MTf activating agent which comprises the steps of:

1) preparing a cell line in which MTf is

- overexpressed, wherein said cell line retains the ability to differentiate to chondrocytes but hardly differentiate without stimulation;
- 2) adding candidate substances to the cell line prepared in step 1) and culturing it for a specified period of time; and
 - 3) examining the cell line for induced chondrogenic differentiation and selecting an MTF activating agent from the candidate substances.

14. (Original) An MTF activating agent obtained by the method according to claim 13.

15. (Original) A chondrogenesis stimulator containing an MTF activating agent obtained by the method according to claim 13.

16. (Currently Amended) Isolated MTF which lacks the GPI anchor region.

17. (New) A method for stimulating cartilage formation comprising administering to a patient in need thereof an effective amount of membrane-bound transferrin-like protein (MTF).

18. (New) The method according to claim 17 wherein the MTF is selected from the group consisting of, human p97 protein and a protein demonstrating MTF activity that has an

amino acid sequence encoded by DNA which hybridizes, under stringent conditions, with a DNA coding for the p97 protein.

19. (New) A method for stimulating chondrogenesis comprising administering to a patient in need thereof an effective amount of membrane-bound transferrin-like protein.

20. (New) The method according to claim 19 wherein the MTF is selected from the group consisting of human p97 protein, and a protein demonstrating MTF activity that has an amino acid sequence encoded by DNA which hybridizes, under stringent conditions, with a DNA coding for the human p97 protein.

21. (New) The method according to claim 19 wherein the patient in need thereof is suffering from a bone disease selected from the group consisting of the following diseases in which chondrogenic differentiation is involved: osteoarthritis; rheumatoid arthritis; injury of cartilage due to trauma; maintenance of chondrocyte phenotypes in autologous chondrocyte transplantation; reconstruction of cartilage in the ear, trachea, or nose; osteochondritis dissecans, regeneration of intervertebral disk or meniscus; bone fracture; and ontogenesis from cartilage.

22. (New) The method according to claim 19 wherein the chondrogenesis stimulator is used in combination with an MTf activating agent.

23. (New) The method according to claim 19 wherein the MTf is selected from the following:

- a. a protein having the amino acid sequence of SEQ ID NO:4 and;
- b. a protein demonstrating the MTf activity that has an amino acid sequence encoded by DNA which hybridizes, under stringent conditions, with a DNA encoding the protein of SEQ ID NO:2.

24. (New) The method according to claim 19 wherein the chondrogenesis stimulator is used in combination with insulin and insulin-like growth factor.

25. (New) The method according to claim 19 wherein the chondrogenesis stimulator is human p97 protein.

26. (New) The method according to claim 19 wherein the chondrogenesis stimulator is soluble isolated MTf.

27. (New) The method according to claim 26 wherein the soluble isolated MTf lacks the GPI anchor region.